

1. Composite semipermeable membrane comprising a semipermeable support membrane and an anticoagulant agent suitable for treating blood and plasma by extracorporeal circulation, characterized in that:
- the semipermeable support membrane consists essentially of a polyacrylonitrile carrying anionic or anionizable groups;
  - the surface of the semipermeable support membrane intended to be placed in contact with the blood or plasma is coated successively:
    - with a cationic polymer carrying cationic groups which are capable of forming an ionic bond with the anionic or anionizable groups of the polyacrylonitrile, the cationic polymer comprising chains whose size is sufficient for them not to pass through the semipermeable support membrane;
    - and with an anticoagulant agent carrying anionic groups which are capable of forming an ionic bond with the cationic groups of the said cationic polymer.
2. Membrane according to Claim 1, characterized in that the anionic or anionizable groups of the polyacrylonitrile are selected from sulphonic, phosphonic, carboxylic, sulphuric, phosphoric groups and from salts of the aforementioned groups.
3. Membrane according to Claim 1, characterized in that the anionic or anionizable groups of the polyacrylonitrile are acid sulphonic groups or salified sulphonic groups.
4. Membrane according to Claim 3, characterized in that the semipermeable support membrane consists essentially of a copolymer of acrylonitrile and sodium methallyl sulphonate.

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5. Membrane according to one of Claims 1 to 4, characterized in that the cationic polymer is a polyamine.

5 6. Membrane according to Claim 5, characterized in that the cationic polymer is a polyethyleneimine.

7. Membrane according to Claim 6, characterized in that the amount of polyethyleneimine deposited is  
10 between approximately 1 mg and approximately 30 mg per m<sup>2</sup> of membrane (including the end points).

8. Membrane according to one of Claims 1 to 7, characterized in that the cationic polymer is prepared  
15 by ultrafiltration using a semipermeable membrane which is identical to the semipermeable support membrane or which has a cut-off threshold equal to or greater than that of the semipermeable support membrane, in order to  
20 exclude the cationic polymer chains capable of passing through the semipermeable support membrane.

9. Membrane according to one of Claims 1 to 8, characterized in that the anticoagulant agent carrying  
25 anionic groups belongs to the family of glycoaminoglycans having an anticoagulant activity.

10. Membrane according to Claim 9, characterized in that the anticoagulant agent essentially consists of  
30 heparin.

11. Membrane according to Claim 10, characterized in that the amount of anticoagulant agent deposited is  
35 between approximately 200 IU and approximately 20,000 IU per m<sup>2</sup> of membrane (including the end points).

12. Exchanger for treating blood or plasma by extracorporeal circulation, comprising two compartments separated by a semipermeable membrane having a surface oriented towards a first compartment intended for the

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circulation of blood or plasma, characterized in that the semipermeable membrane is a composite semipermeable membrane according to one of Claims 1 to 11, and in that the surface of the membrane oriented towards the first compartment is coated successively with a cationic polymer and with an anionic anticoagulant agent.

13. Exchanger according to Claim 12, characterized in that the composite semipermeable membrane is a flat membrane.

14. Exchanger according to Claim 12, characterized in that the composite semipermeable membrane consists of a bundle of hollow fibres.

15. Method for reducing the thrombogenic character of an exchanger for treating blood or plasma by extracorporeal circulation, comprising two compartments separated by a semipermeable membrane having a surface oriented towards a first compartment intended for the circulation of blood or plasma, the method comprising the following successive stages:

(a) preparing a semipermeable membrane, in the form of a flat membrane or a bundle of hollow fibres, from a solution of polyacrylonitrile carrying anionic or anionizable groups;

(b) assembling the various components of the exchanger, in particular fitting the semipermeable membrane or a bundle of hollow fibres in a case;

(c) preparing a solution containing at least one cationic polymer carrying cationic groups which are capable of forming an ionic bond with the anionic or anionizable groups of the polyacrylonitrile, the cationic polymer comprising only polymer chains whose size is sufficient for them not to pass through the semipermeable membrane, and bringing this solution into contact with the surface of the semipermeable membrane intended to be placed in contact with the blood or

plasma, it being possible to carry out stage (c) before or after stage (b);

(d) in the event that stage (c) is carried out subsequently to stage (b), purging the exchanger of the solution containing the cationic polymer;

(e) preparing a solution containing, in the dissolved state, at least one anticoagulant agent carrying anionic groups which are capable of forming an ionic bond with the cationic groups of the said cationic polymer, and bringing this solution into contact with the surface of the semipermeable membrane intended to be placed in contact with the blood, stage (e) being implemented after stage (c) but before or after stage (b);

(f) in the event that stage (e) is carried out subsequently to stage (b), purging the exchanger of the solution containing the anticoagulant agent.

16. Method according to Claim 15, characterized in that the semipermeable membrane is rinsed in order to remove the excess unbound cationic polymer, either after stage (c) when stage (c) is carried out before stage (b), or after stage (d).

17. Method according to Claim 15 or 16, characterized in that the semipermeable membrane is rinsed in order to remove the excess unbound anticoagulant agent, either after stage (e) when stage (e) is carried out before stage (b), or after stage (f).

18. Method according to Claim 15, 16 or 17, characterized in that the exchanger is sterilized when the semipermeable membrane based on polyacrylonitrile carrying anionic or anionizable groups is coated with the said cationic polymer, then the treatment using the solution containing at least one anticoagulant agent is performed extemporaneously.

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19. Method according to Claim 15, 16 or 17, characterized in that the exchanger is sterilized when the semipermeable membrane based on polyacrylonitrile carrying anionic or anionizable groups is coated with  
5 the said cationic polymer and the said anticoagulant agent.

20. Method according to Claim 15, characterized in that the cationic polymer is prepared by  
10 ultrafiltration using a semipermeable membrane which is identical to the semipermeable support membrane or which has a cut-off threshold equal to or greater than that of the semipermeable support membrane, in order to exclude the cationic polymer chains capable of passing  
15 through the semipermeable support membrane.

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